**NIH application: Non technical abstract/draft 1.0**
**REGENT I**

Gene transfer is a potential therapy in which a specific gene is introduced into target cells. The transferred gene typically carries information for specific enzymes or other biological factors that are required for normal functioning or regulation of the organs or systems. CAR-MP583, the material proposed for use in this REGENT I clinical trial, contains a gene that induces the formation of an enzyme, which in turn increases the amount of nitric oxide (NO). Nitric oxide is normally produced in the wall of blood vessels. Many scientists think that a decrease in the production of NO in the vessel wall reduces the protective function of the inner lining of the blood vessel and that this may contribute to the process of renarrowing of the artery after it has been treated. Therefore, treatment with the gene for iNOS may increase the amount of NO in the wall of the heart artery and decrease the chances for this artery to renarrow. If the iNOS gene transfer procedure is successful in preventing or diminishing re-narrowing of cardiac blood vessels, the requirement for additional treatment of the narrowed, stented artery by either angioplasty or a surgical procedure may be reduced or eliminated.

The iNOS gene is administered in a lipoid fluid. Together the gene and the lipoid fluid are called a lipoplex. In animal studies with the iNOS-lipoplex gene product (given directly into the arterial wall before the vessel was experimentally narrowed) less arterial narrowing was seen. This potentially beneficial effect was not associated with undesirable effects.

The iNOS-lipoplex gene product will be applied directly into the inside wall of the narrowed artery by using a special device called the Infiltrator® catheter, which has a small balloon with microports on its surface. When the balloon is inflated, the micro-ports enter the arterial wall in the narrowed region and the gene transfer product is injected. The FDA has not yet approved the Infiltrator®; however it is being used in other research studies with the full knowledge of FDA. So far, studies in animals and human beings have shown that the device can be used to deliver drug into the artery wall.
No complications or toxicity were associated with the iNOS-lipoplex gene product during the animal studies.

All the risks of using the Infiltrator® device are not known, but they are believed to be similar to those associated with the standard balloon angioplasty treatment for a blocked coronary artery. The device may tear the inner lining of the blood vessel. This result also is commonly seen after the use of other balloon angioplasty catheter devices. Self-expanding mesh devices (stents) are routinely used in most heart catheterization procedures, and they are the standard treatment for tears. Stents are required to be used in the REGENT I study, whether or not a tear has occurred. The materials used to manufacture the Infiltrator® are similar to other balloon angioplasty catheters and are not considered toxic.

Because the iNOS-lipoplex gene product is an investigational drug, there could be unforeseen risks. To assure appropriate monitoring of patient safety, physicians experienced in heart catheterization procedures will evaluate the undesirable effects in the study. The decisions of these heart doctors will then be reviewed by an independent group of doctors who are experts in the conduct of gene therapy clinical trials.